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CHILDREN'S HOSPITAL

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MENINGOCOCCEMIA

Case Report No. 44

Dr. Charles Stiegler M. Z.—46-649

This is the case of M. Z., a 4 year old white female who was admitted to the hospital on January 25, 1946 at 5 a.m. because of high fever. The patient had been well until the evening prior to admission at which time the parents noticed the child was becoming drowsy and feverish. Upon consulting a doctor hospitalization was advised. There was no history of an antecedent respiratory infection or convulsions. The remainder of the history was non-contributory.

On admission, physical examination revealed a well-nourished, well-developed, critically ill white female in a semi-comatose condition. The temperature was 106° (R), pulse rate 130 per minute, respiratory rate 36 per minute. There were a moderate number of petechiae, pinpoint size, scattered over the upper and lower extremities, with a lesser number present on the chest and abdomen; they did not blanch on pressure. The pupils were dilated and equal bilaterally and reacted to light and accommodation. The pharynx was slightly injected. Examination of the lungs, heart and abdomen revealed no abnormalities. There was moderate nuchal rigidity and hyperactive reflexes on the left; no other neurological abnormalities were found.

A petechial smear taken on admission showed many gram negative diplococci, mostly extracellular, morphologically resembling meningococci. A hemogram taken on admission showed 11 gms. of hemoglobin, 3.80 million red cells, 2,400 leucocytes with many toxic neutrophiles. The urinalysis showed an albuminuria of 30 mgms. A blood culture taken on admission was positive for Neisseria intracellularis, Group I, on January 28th. A spinal tap was done, yielding clear fluid under no increased pressure and 10,000 units of penicillin were administered intrathecally at this time.

Treatment was instituted with 100,000 units of penicillin being given intramuscularly stat, and 50,000 units intramuscularly every 3 hours. The patient developed a mild generalized convulsion at this time, which was controlled with phenobarbital. Sodium sulfadiazine, grams 2½ in 300 c.c. 5% glucose, was given by venous infusion, followed by half this dosage every 6 hours in 150 c.c. of saline. The patient received 2 c.c. adrenal cortical extract I.M. and 1 c.c. of caffeine sodium benzoate. At this time, 7 a.m., the patient's condition was poor, she was very toxic with a notable increase in the amount of the rash present and the size of the lesions. The

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temperature was 102° and the blood pressure was 60/10. The diagnosis at this time was Meningococcemia, possible Waterhouse-Friderichsen Syndrome.

Chemotherapy was continued, and adrenal cortical extract was increased to 5 c.c. every 3 hours for four doses. The patient also received 300 c.c. plasma, 300 c.c. $\frac{1}{6}$ molar lactate solution, and 150 c.c. blood. At 4:30 p.m. on the day of admission, her condition improved slightly; she was restless, irritable, but no longer in coma. The blood pressure was 70/40, temperature 101°. Nuchal rigidity and positive Kernig and Brudzinski signs were present at this time. The patient was taking and retaining fluids by mouth. The white blood-count was repeated at this time, and showed 10,000 leucocytes, 79% neutrophiles, 3% eosinophiles, 18% lymphocytes; no abnormalities of the cells were noted, and the platelet count was normal. The sulfadiazine level was 16.2 mgm./100 c.c.

The temperature was normal the morning of January 26th, and the patient's condition was remarkably improved; she was fully rational and her blood pressure was 86/64. The white blood-count had risen to 20,700 with 87% neutrophiles and 12% lymphocytes. Penicillin was reduced to 25,000 units intramuscularly every 3 hours. The rash had faded by January 27th, and on January 28th the therapy was changed to oral sulfadiazine gr. 7.7 every 4 hours. A hemogram on January 31st was normal and the penicillin was discontinued at that time. The sulfadiazine was discontinued on the 8th day of the patient's hospitalization.

Second Case

R. D.—46-648

This is the case of a $3\frac{1}{2}$ year old white male who was admitted to the hospital January 25, 1946 at 1:30 a.m. because of high fever and drowsiness of 6 hours duration. The patient had complained of a slight headache throughout the afternoon of January 24th but was apparently well until 4 p.m. that afternoon. At this time he began to complain of pains in his hands and feet; they were sensitive to touch. The child was given empirin compound, without any relief. During the evening the child began to feel hot to touch, was restless and at times "out of his head". About 10 p.m., his family noticed a rash appearing on his body. As his condition seemed to be getting worse, he was brought to the hospital admitting room. Past history and family history are irrelevant.

When seen in the admitting room, the patient was a well-nourished, well-developed $3\frac{1}{2}$ year old white male, acutely ill, drowsy, very pale, respirations rapid but not labored. The temperature was 103° by rectum. A petechial rash was scattered diffusely over the face, extremities, and entire trunk; the lesions were pin-head size, red, raised, and did not blanch on pressure.

The nasopharynx was slightly injected and there was mild nuchal rigidity, but the remainder of the physical examination was negative. Because of the serious condition of the patient, the acuteness of the process, a marked petechial rash, nuchal rigidity, and fever, a tentative diagnosis of meningococcemia, possible Waterhouse-Friderichsen Syndrome, was made. A blood culture, complete blood count, and petechial smear was taken in the admitting room. The patient was then given 100,000 units of penicillin.

When the patient had been transferred to isolation from the admitting room, it was noted that the rash was becoming confluent, with purpuric areas being present on the buttocks. Because of the critical condition of the patient, a spinal tap was not done. The petechial smear was reported at that time as evidencing many gram negative extra and intracellular

FIG. 1. R. D. OVERWHELMING MENINGOCOCCEMIA WITH HEMORRHAGE INTO THE ADRENAL GLANDS
Note the extensive petechial rash

diplococci, morphologically resembling meningococci. The hemogram taken in the admitting room showed hemoglobin 10 grams, erythrocytes 3,200,000, and leucocytes 2,850 with many toxic forms of neutrophiles. Treatment consisted of general supportive measures and: 1) penicillin 50,000 units every three hours, 2) sodium sulfadiazine, one ampoule in 300 c.c. of 5% glucose in Hartman's solution intravenously; ½ ampoule in 150 c.c. of 5 per cent glucose in Hartman's by clysis every six hours, 3) adrenal cortical extract 2 c.c. intramuscularly every three hours. The patient became increasingly toxic, with alternate periods of restlessness and drowsiness. The rash continued to spread and became hemorrhagic and purpuric in character. The blood pressure was 80/58. Respirations became increasingly labored and the patient was placed in an oxygen tent at 3 a.m. A transfusion of 250 c.c. blood was started but the child died at 5 a.m. after receiving about 75 c.c.

The patient had been under treatment approximately four hours and had received 150,000 units penicillin intramuscularly, adrenal cortical extract 4 c.c. intramuscularly, sodium sulfadiazine 2.5 grams intravenously in addition to general supportive therapy. The final diagnosis was overwhelming meningococcemia and adrenal collapse. The blood culture taken on admission yielded meningococcus, group II.

Post-mortem examination on January 25, 1946 revealed the presence of petechial hemorrhages into the skin, conjunctiva, pleura, pericardium,

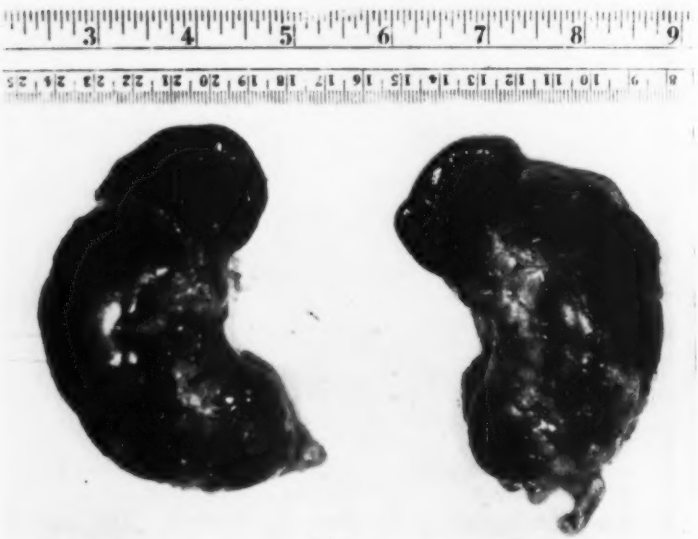

FIG. 2. R. D. EXTENSIVE HEMORRHAGE INTO THE ADRENAL GLANDS ASSOCIATED WITH MENINGOCOCCEMIA

and peritoneum. Both adrenals were approximately three times their normal size, and were the sites of massive, infiltrating hemorrhages. There were no other significant abnormalities found. Cultures taken at post-mortem were as follows: a) heart's blood, meningococcus, group II, b) cisternal fluid; smear negative, no growth obtained, and c) spleen; smear negative, no growth obtained. Cisternal fluid examination revealed a slightly cloudy fluid with: a) protein; 60 milligrams %, b) sugar; no reduction of Benedicts in five hours, and c) cells; 64 with 56 polymorphonuclears, 42 lymphocytes and 2 endothelial cells.

Discussion

Two cases of severe meningococcemia have been presented to illustrate the similarity in their clinical picture on admission to the hospital, and the dissimilarity of their course under identical treatment. We believe this to be the result of severe hemorrhage into the adrenal in the case of R.D. with the concomittant production of the Waterhouse-Friderichsen syndrome; and the absence of this factor in the case of M. Z., who went on to eventual recovery.

On admission to the hospital, both cases were tentatively diagnosed as severe meningococcemia, possibly Waterhouse-Friderichsen syndromes. Blood cultures were positive for Neisseria meningococcus in both cases, group II in the case of R. D., and group I in the case of M. Z. The onset in both cases was acute, with emphasis on the high fever and the appearance of a rapidly spreading petechial rash. In neither case were there signs of marked meningeal involvement, but rather the picture of an overwhelming septicemia, each semicomatose patient having a high fever and a profuse petechial rash which tended to become confluent. A marked leucopenia and the presence of gram negative diplococci in the petechial smears were likewise present in both cases. It should be pointed out again that the leucopenia present in these cases is no contraindication to the use of large doses of sulfones intravenously. When the toxic suppression of the bone marrow is overcome by chemotherapy, a leucocytosis in keeping with the septicemia present becomes apparent.

The treatment instituted in both cases was similar in nature, consisting of chemotherapy and general supportive measures. In the case of R. D. the course was progressively downhill, with the body surface assuming more and more a postmortem lividity until exitus occurred. In the case of M. Z. the course was downhill for 5–6 hours with the rash becoming more confluent and the patient becoming delirious; after this the patient began to show slow improvement over the next 12 hours and then further improvement was strikingly rapid.

In a review of 15 cases of Waterhouse-Friderichsen syndrome seen at Children's Hospital previously, N. intracellularis was established as the etiological agent of the septicemia in 10 cases, N. flava II in one case, and Hemophilus influenza in 2 cases; the bacterial agent was not established in two cases. In all but one case the onset was acute, being a matter of hours until the patient was admitted to the hospital in a critical condition. Hyperpyremia, petechial rash, a gradually spreading cyanotic hue to the skin associated with manifestations of increasing peripheral vascular collapse was characteristic. Neurological manifestations were not marked. Seven cases occurred prior to 1940 and were treated only with general

supportive measures; in one of these cases meningococcal antitoxin was given. The remaining 8 cases occurred in 1944 and 1945; these cases were treated with combined chemotherapy (penicillin and sulfones), adrenal cortical extract, and general supportive measures. All 15 cases pursued a downhill course ending in death.

Postmortem examination was done in all cases. In each there was moderate to massive hemorrhage into cortical and medullary regions of the adrenals. Petechial hemorrhages scattered throughout the skin surfaces and the gastro-intestinal tract was characteristic.

Summary

1. Two cases of severe meningococcemia with similar clinical pictures from onset until hospitalization have been presented.

2. Treatment in both cases was similar; one case made a dramatic recovery while the other case terminated fatally.

3. We believe this to be the result of adrenal hemorrhage in one instance, and the absence of any notable adrenal involvement in the case of M. Z.

*Special Report**

THE PROBLEM OF THE CHILD BORN OF A DIABETIC MOTHER

Dr. Edwin Blair

In discussing the various pediatric problems and emergencies that may result when a diabetic mother gives birth, it must be realized that a sharp line of distinction between the spheres of obstetrics and pediatrics will only serve to increase the difficulties already present, and may also create new ones. The pediatric care of such an infant must be begun during the mother's pregnancy and continued into the postnatal period, the former being carried out by the obstetrician, and the latter by the pediatrician. And aside from the care of the infant, the pediatrician must be aware of the factors involved in the management of the pregnant diabetic woman which may in turn create for him new difficulties. Many of these factors will be discussed later.

The first problem, or set of problems to be analyzed, are those resulting from the almost inevitable obstetrical difficulties. One set of statistics gives the incidence of breech presentations in diabetic pregnancies as being at least 33%. These breech presentations in the presence of an atonic uterus, which is so frequent an accompaniment of a diabetic pregnancy, may present the following:

1. Asphyxia. This may be due to prolapse of the cord; twisting of the cord, either spontaneously or as a result of manipulative procedures designed to correct the breech; premature separation of the placenta—the increased frequency being due to a more rapid aging of the placenta and also to the manipulation used on the breech; delayed passage of the fetus due to the uterine inertia as well as the large size of the infant.
2. Fractures. The common sites for fractures are the skull and clavicles. These occur as a result of trying to pass the macrosomatic infant through the birth canal. They may also be due to the instrumentation used to deliver the baby, and finally, the haste with which many of these infants are delivered, either for their own distress or that of the mother, is a factor involved in the production of some of these fractures.
3. Intra-cranial Hemorrhage. The obstetrical pathogenesis is the same as that for fractures with the exception that the malleability of the skull may permit considerable trauma to the intra-cranial structures without actual fracture of the skull.

*Student competitive essay.

While the three factors mentioned above may complicate any pregnancy, I shall attempt to show, in a later discussion, the chemical and physiological mechanisms that tend to make for increased frequency in babies of diabetic mothers. These mechanisms are extremely complex and the entire interrelationship is still in the process of being evolved. Many of the theories that are to be discussed do not have the unanimous support of the workers in the field, but they at least indicate a trend and make an attempt to answer hitherto unanswerable questions.

One of the more frequently observed abnormalities occurring in infants of diabetic mothers is macrosomia. Its rôle in affecting the infant has already been discussed. Its mechanism is explained by Kurzrok as follows:

The use of insulin in the control of the mother's diabetes plus the insulin excess produced by the normal fetal pancreas result in a markedly increased carbohydrate metabolism. This, in turn, results in a great deal of water being formed in the tissues of the fetus (as well as the mother). Adding to this difficulty, is the retention of salt which he believes occurs. He offers as proof the fact that when insulin is discontinued, there is no increased excretion of water, the explanation being that the salt, accumulating in the tissues, holds water with it. Therefore, it would seem that the macrosomia is due to two or possibly three factors. One of these is the excessive deposition of fat, resulting from the storage of large quantities of carbohydrate which reach the infant from the maternal circulation through the placenta. This, of course, results from a failure of the mother to utilize carbohydrate adequately. The second factor is that of edema, the mechanism for which was given above. The third factor is one which is not frequently considered in discussions of macrosomia. It is simply the fact that a diabetic pregnancy frequently has a prolonged period of gestation. This in itself is sufficient to considerably increase the size of the baby. The treatment of the infant during the pregnancy is that of extremely close regulation of the diabetes in the mother, with care being taken to keep the mother's blood sugar as nearly normal as possible. After birth, when the infant no longer must combat the mother's disordered carbohydrate and endocrine imbalance, the obesity and edema should take care of themselves with the baby on a normal diet.

Another, though harmless problem which is less frequently seen, is that of menstruation in the new-born infant. While this situation is of no consequence, it is rather disturbing to the parents and requires explanation. This is not more common in diabetic pregnancies per se, but it is more common in the children of diabetic women who have received estrogen therapy. In this treatment, large doses are used which build up the endo-

metrium of the infantile uterus. When the baby is born, the estrogen levels drop, and the hyperplastic endometrium is shed just as the adult endometrium is lost in a mature woman. Also involved in the use of estrogens are the breasts of the new-born. These are frequently engorged, and this condition may be associated with the secretion of the so-called "witches milk". Again, the condition is perfectly harmless, and only care to prevent mastitis and reassurance to the parents are all that are necessary.

One of the most interesting studies of infants born of diabetic mothers has been made by Miller, Roswell, and Durlacher. They have made a comparative study between such infants and those with erythroblastosis fetalis. The similarity between the two apparently widely separated conditions, is striking. Findings which were formerly believed to be only present in children of diabetic mothers are found in erythroblastotic babies, and similarly, purely erythroblastotic infants showed many of the characteristics of those born of diabetic mothers. The following features were found to be common to both conditions:

1. Circulating erythroblasts
2. Cardiac hypertrophy
3. High myocardial glycogen
4. Hepatic erythropoiesis
5. Edema
6. Jaundice
7. Hyperplasia of the Islets of Langehans
8. Macrosomia

Of course, all of these findings do not occur in each and every case of the disease but their occurrence is undisputable. And what is even more striking, is the fact that *these findings occurred in infants whose mothers did not develop signs and symptoms of clinical diabetes until as much as fifteen or twenty years after the delivery* (that is, after having a non-diabetic pregnancy). The actual significance is as yet unknown, but the facts presented above may help to explain part of the confusion that still exists when the problem of erythroblastosis comes up. There occasionally is seen a case of erythroblastosis fetalis in which the usual antigen-antibody set-up does not obtain. That is, anti-Rh antibodies cannot be demonstrated in the maternal circulation. Even the various sub-groups of the Rh factor do not seem to play a part. We can imagine, then, that this erythroblastotic picture (which admittedly can be varied to account for the picture of Icterus Gravis, Hydrops Fetalis) may be entirely due to a situation like that described above, in which the mother has not yet developed diabetes but where the infant nevertheless shows the "typical" picture of erythroblastosis fetalis. It is difficult for me to account for the pleomorphic picture of erythroblastosis even on the basis that one of the characteristics of the disease may predominate over the others. It is easier for me to postulate that some, at least, are due to an infant born of a *future diabetic woman*. I have not seen such studies made, but it would be interesting

to follow up the mothers of "erythroblastotic" infants to see what percentage of them later developed diabetes.

The presence of hyperplasia of the islets of Langerhans suggests an interesting relationship between this early activity and the future formation of pancreatic adenomas. The fetal pancreas is subject to marked fluctuation of activity. This is, of course, due to the mother's inability to handle her own glucose properly. This alternation of periods of activity with those of inactivity may be analogous to the situation that occurs in the thyroid. It is believed that variation of activity causes first hyperplasia and then involution. This process, repeated over a long period of time eventually leads to adenoma formation. The fetal pancreas in a diabetic pregnancy may follow a similar pattern. A study is indicated to determine the incidence of pancreatic adenomas in patients who have been born of diabetic mothers. This study would be extremely difficult to carry out for several good reasons. First, the frequency of occurrence of these adenomas is rare. Second, the lag that may occur between the birth of the child and the recognition of diabetes in the mother would result in many cases being missed, either through failure to follow the woman long enough, or because of death occurring in the interim.

Stemming from the discussion of fluctuation of fetal pancreatic activity is the question of whether or not insulin can pass the placental barrier. This point has been discussed pro and con for many years. Pack and Barber say that insulin can pass. Corey also agrees. Olow states that it can not pass, while Aron maintains that it does pass in the latter part of pregnancy. Apparently, most men believe that it does cross the placenta. They offer as proof, the fact that many diabetic women show marked improvement after the development of the fetal pancreas. However, this could be easily explained by the fact that the glucose itself diffuses through the placenta and is acted upon by the fetal insulin in the fetal circulation. I believe that I can offer a kind of proof to support the contention that insulin does not pass the placenta. This "proof" is not an experimental one but is merely a theoretical one and has not been offered by any one, so far as I have been able to learn.

In using glandular products as therapeutic agents, it is generally held by physiologists that using estrogens, for example, does not stimulate the ovaries to produce more. In fact the reverse is considered to be the case, that is, the administered estrogens tend to depress the natural secretions. This is generally true of all replacement therapy. So it is in the case of the pancreas. If in the course of treatment of the diabetic woman, the insulin given her were to pass through the placenta, the insulin secretion of the fetal pancreas should be depressed by the time the baby is born. But this is not the case. In fact, the opposite is true. Babies born of diabetic

mothers almost invariably have excessive activity of the islet cells as evidenced by the accompanying hypoglycemia. There are many loopholes in this argument, but it is merely offered as a suggestion.

The hypoglycemia itself offers some difficulty in the care of the new-born. It must be distinguished from other possible causes of unconsciousness, especially intra-cranial hemorrhage, and asphyxia, both of which must be carefully considered in diabetic pregnancy. It seems reasonable to administer glucose to all babies born of diabetic mothers. If the glucose is not needed then no harm is done. On the other hand, if it is a hypoglycemia that is causing the difficulty, then the glucose will be both an aid in diagnosing the case as well as a life-saving procedure.

The upset hormonal imbalance which diabetic mothers have is responsible in at least one way for the poor nourishment of the new-born infant. These mothers almost invariably fail to lactate. The percentage reaches almost 100%. The reason for this failure is as follows:

It has been adequately determined that one of the essentials in the institution of satisfactory lactation is the secretion of prolactin by the anterior lobe of the pituitary. This hormone is inhibited in normal pregnancies by the presence of high concentrations of estrogens. The prompt fall of these levels in the first few days post-partum removes this inhibition, and allows the prolactin to act. In the diabetic woman there is no such drop because the estrogen levels are low to begin with. This is due to atrophy and poor follicular development of the ovaries of the diabetic woman. The important factor than, is the drop in titer, rather than the actual level. And since the drop does not occur, lactation fails. This failure is especially important in areas where the proper infant care is not available and where human milk is not readily obtained. Add to this the fact that many of these infants are born prematurely, due to maternal accidents, and it is readily seen that the risks of fetal mortality are increased.

In attempting to review the problem of the child born of a diabetic mother, I have stressed the most important mechanisms and physiological processes involved, and have shown their effect upon the well being of the infant. This paper, by no means, covers the entire field, nor is it possible to do so at the present time. There still remains a great deal of both statistical and experimental work to be done before all the interrelationships, effects, treatments, and prophylaxis can be worked out. For example, in the diabetic mother, it is not the pancreas alone that is at fault. There are many other glandular disturbances such as thyroid, pituitary, and adrenal dysfunction. Certainly these disturbances must play a rôle in determining the eventual outcome of the infant even into adult life. The amount of information already accumulated is minimal compared to that which is still awaiting discovery. With the knowledge at hand, certain precautions

may be taken even now to help reduce the mortality to the lowest possible level.

1. Treat the mother from the onset of her pregnancy with the best of care possible, including estrogen therapy.
2. Have available for immediate use, a resuscitator, preferably of the Kreislman type.
3. Give all infants born of diabetic mothers glucose as prophylaxis against hypoglycemia.
4. Distinguish hypoglycemic shock from other causes of unconsciousness.
5. Make every effort to distinguish the infant of a diabetic mother from a baby suffering from erythroblastosis fetalis, even if only to keep accurate statistics. These records may eventually help explain the puzzling similarity between the two conditions.
6. Every case is *a* case and not a *series* of cases. Each must be carefully considered individually.

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SPONTANEOUS PNEUMOTHORAX

Case Report No. 45

Dr. James M. Moser

On January 17, 1946 a four month old colored male was admitted to the Children's Hospital in a cyanotic, semi-stuporous condition with marked respiratory irregularity. His mother stated that he had been perfectly well up until 7:30 p.m. of the day of admission. Returning to his room, after being absent for 15 minutes, she found him lying on his back with his hands over his head, his neck retracted, cyanotic and limply unconscious. She immediately picked him up and "blew into his face." This seemed to help him get his breath. She noted at the time that considerable foam was present about his mouth.

The child was brought to the hospital as quickly as possible, remaining limp and cyanotic during the trip and breathing with difficulty and irregularity. There had been no convulsions, muscle twitching, vomiting, diarrhea or previous "cold."

The past history, feeding history and family history were non-contributory.

Physical examination revealed a well-developed, well-nourished 4 month old colored male in severe respiratory distress. He was cyanotic and the respirations were irregular being rapid for a while then very slow and hesitant. Examination of the chest was negative, the only positive finding being bilateral ankle clonus.

An x-ray plate of the chest was made on admission and revealed a diffuse infiltration throughout both lungs. The child was given caffeine sodium benzoate and coramine subcutaneously and placed in an oxygen tent. Within three hours his condition had improved and his respirations became regular with a definite improvement in the cyanosis. The rectal temperature taken at this time was 102°F. The child remained in this condition through the night.

On the morning after admission further examination revealed three plus rigidity of the neck, rapid shallow respirations, diminished breath sounds all over the left chest with some hyperresonance, increased and harsh breath sounds over the right upper lobe anteriorly and bilateral ankle clonus.

An x-ray of the chest (taken 18 hours after admission) revealed a left pneumothorax and an opacity involving the upper half of the right lung field. A blood count taken at this time revealed a leukocyte count of 14,100 with 63% segmented forma and 37% lymphocytes. Urinalysis

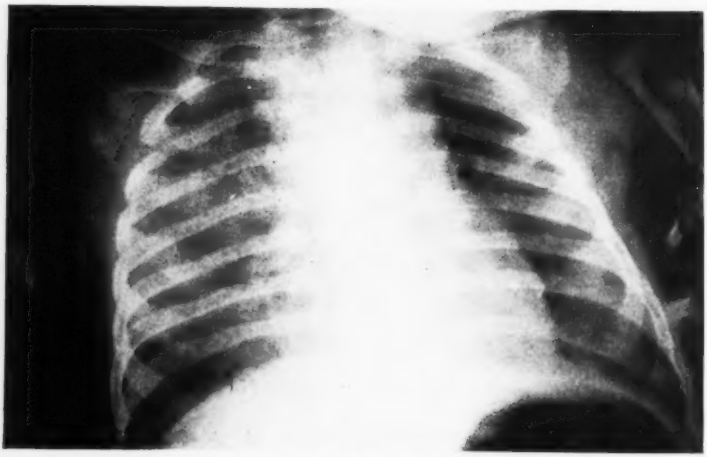

FIG. 1. A. N. D. THIS X-RAY WAS TAKEN UPON ADMISSION AND REVEALS HAZINESS THROUGHOUT THE RIGHT LUNG BUT APPARENTLY NORMAL PARENCHYMA ON THE LEFT

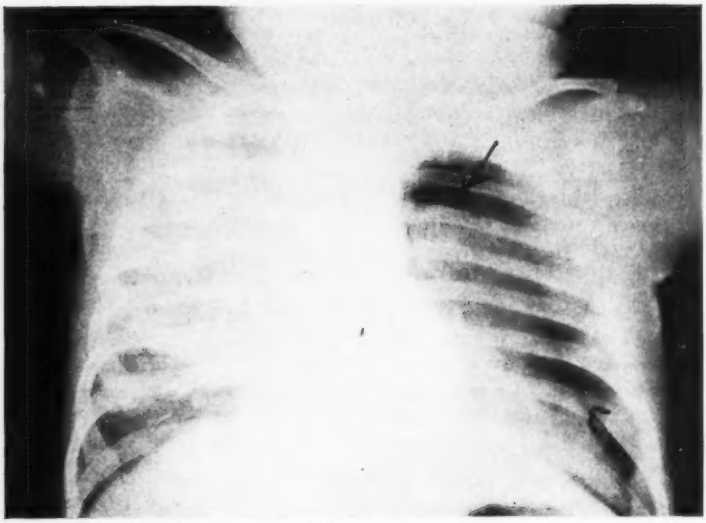

FIG. 2. A. N. D. X-RAY TAKEN 18 HOURS AFTER THE PREVIOUS PLATE SHOWING PNEUMOTHORAX ON THE LEFT

was essentially negative. Spinal fluid examination was negative as were the old tuberculin and P.P.D. #1 skin tests.

The child was given 20,000 units of penicillin intramuscularly stat and

10,000 units every 3 hours. He was given fluids parenterally in the form of subcutaneous clyses every 3 hours.

Dr. Klepser was called in consultation and he saw the child about 2:30 p.m. the day after admission. He felt that it was not necessary to aspirate any air because the child's left lung seemed to have re-expanded and he had no repiratory difficulty after being out of oxygen for 15 minutes. He advised observation.

On the morning of January 19, 1946, 2 days after admission, the patient looked markedly improved. His color was much better and he began to take his formula well. There were fine rales and bronchial breathing in

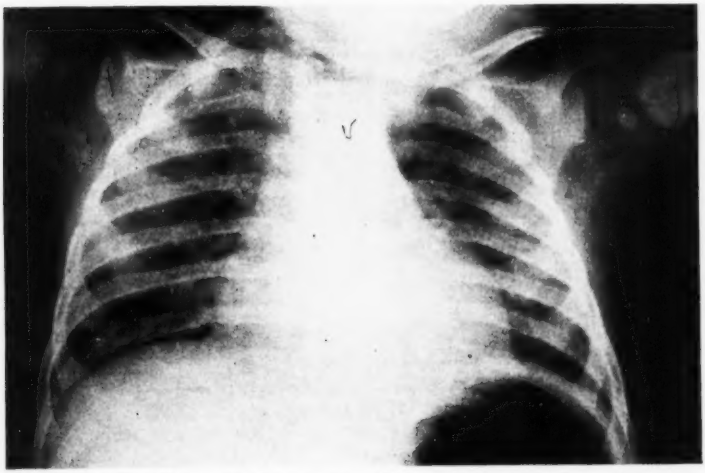

FIG. 3. A. N. D. COMPLETE SPONTANEOUS EXPANSION OF THE COLLAPSED LUNG AFTER SIX DAYS

the right upper lobe anteriorly and the ankle clonus had disappeared. The oxygen tent was discontinued along with the clyses.

An x-ray of the chest was taken on January 19, 1946 which revealed considerable re-expansion of the left lung with the mediastinum in normal position and the homogenous density still present in the upper half of the right lung. The temperature came to normal by lysis on the sixth hospital day and stayed there. The child continued to show improvement with an essentially clear chest x-ray on January 23, 1946, and was discharged as recovered on January 28, 1946.

DISCUSSION

Dr. Clifford J. Tichenor: Here we have had an unusual opportunity to observe clinically and radiographically an infant presenting essentially a

picture of spontaneous pneumothorax. The etiology of this phenomena must remain nebulous, but the causes of pneumothorax are an interesting problem.

Air may gain access to the thoracic cavity either by wounds of the thoracic wall or by rupture of the lung into the pleural cavity, such as may occur in chronic ulcerative tuberculosis or other forms of tuberculosis of the lung, abscess, gangrene, tearing of the lung by fractured ribs or by exploratory needles, suppurative types of pneumonia, infected infarcts; and it is said to occur from ruptures of an emphysematous lung or a normal lung with an extreme expiratory effort in coughing, etc. It is also reasonable to postulate that rupture of a congenital bleb originating in the pleura might allow air to gain access to the thoracic cavity. Gas forming bacteria may also lead to the presence of gas in the pleural cavity. External wounds which remain open may lead to so called open pneumothorax. Ruptures of diseased lungs may close down leaving a closed pneumothorax, or the tissues around the opening may operate in a valve-like fashion so that air enters during inspiration and cannot be expelled completely during expiration. In general communications of this latter type, valvelike or not, are called bronchopleural fistulas. Infection occurs rapidly and as usually seen the condition is a pyopneumothorax.

It is well known that pneumothorax may be complicated by an interstitial emphysema of the lung, either following the rupture of diseased lungs or by the same trauma that caused the pneumothorax. Similarly, interstitial emphysema of the thoracic wall may occur, usually localized but sometimes extending up in the neck and down over the abdomen.

Pneumothorax is rare in children, and sometimes cases are encountered for which no explanation can be found. Aspiration of a foreign body should always be considered and ruled out.

It is interesting that the physical signs and symptoms do not differ remarkably from acute adult pneumothorax. The onset is usually sudden with rapid respiration and cyanosis, and when respiratory disease already exists these symptoms may be marked. Careful attention should be paid to repiratory lag in an affected side, to tympanitic percussion, to distant breath sounds and displacement of the heart. When the typical coin sound is obtainable the diagnosis is usually already apparent.

The mortality with pneumothorax in young children is high, being about 50%; death mostly results from the associated conditions and not from the pneumothorax itself.

REFERENCE

Bovaird: Pneumothorax in Children. Arch Pediatrics, **20:** 817, 1903.

CLINICAL PATHOLOGICAL CONFERENCE

Directed by: Dr. E. Clarence Rice

Assisted by: Dr. Robert B. Sullivan

Case Report No. 46

Dr. Robert Sullivan

We are presenting the case of a white male infant who was born at term by a normal delivery. The birth weight was six pounds and two ounces. Because he was "born with almost complete atelectasis" he was kept in high concentration of oxygen for three days. Thereafter he seemed to do well until he was two weeks old when he was admitted to Children's Hospital because of an episode of "complete stoppage of respiration" and cyanosis. He was fairly well-developed and well-nourished, was in respiratory distress with an expiratory wheeze. There were distant breath sounds in the right chest. An interpetation of the roentgen studies suggested atelectasis on the right with a shift of the mediastinum to that side. After one week the mediastinum was in the mid-line but there was a triangular area of increased density in the fourth left intercostal space which was thought to be inflammatory in nature. Three days later he was discharged.

He was again admitted when five weeks old because of dyspnea of twelve hours duration. There was sternal retraction with each inspiration, decreased breath sounds in both lungs with occasional rales. The complete blood count was normal except that there were 5.45 million red blood cells per cu. mm. X-ray studies on admission indicated an atelectasis of the lower left lobe and a mass in the posterior mediastinum from the second to the fifth interspace which displaced the trachea anteriorly and to the right. During a four week period a total of seven hundred roentgen units of X-ray therapy were directed at the mediastinal mass. The left lower lobe re-expanded and a diffuse haziness was reported over the right lung field which may have been due to the X-ray therapy. The mass became somewhat smaller and he was again discharged but continued to have moderate respiratory distress.

When two months old he was admitted for the last time because of cyanosis of one day's duration. He was poorly nourished and cyanotic. Dyspnea and wheezing were constant and there were periods of apnea which necessitated artificial respiration. An oxygen tent was employed continuously. The complete blood count was within normal limits and throughout the illness there was never more that sixth-tenths of a degree of fever. X-rays taken on this admission were reported to show the retropharyngeal

space to be normal. The trachea was still displaced anteriorly by the same mass described before. There was an increase in fibrosis throughout the right chest and emphysema in both bases. Eighteen days after this admission he died during one of the apneic episodes.

Necropsy Summary

The left lung was completely collapsed and the right lung was markedly emphysematous. The atelectatic left lung was apparently due to a cystic

Position of the Cyst Arising from the Trachea and Left Main Bronchus

mass measuring 2 x 3 c.cm. which arose from the posterior wall of the carina and extended downwards along the left main stem bronchus. This mass contained 8 c.cm. of grayish thick mucous material which upon microscopic examination showed a few cholesterol crystals but no cells. The mass itself was grayish white in color and had a smooth lining. On section, the cyst was composed of crescents of fibrous tissue lined with well-differentiated bronchial epithelial cells, none of which were ciliated. The posterior wall of the left main bronchus was deficient of cartilage which resulted in obstruction of this bronchus by the mass when it pressed forward.

Differential Diagnosis

Dr. R. W. Alman

This child's trouble consisted of a series of acute attacks of respiratory distress, caused by obstruction of the airway. A discussion of the various causes of acute dyspnea and cyanosis is unnecessary in this case, for the X-ray conclusively demonstrates anterior displacement and partial compression of the trachea. The differential diagnosis devolves, therefore, upon the identification of a posterior mediastinal mass. Intrathoracic tumors are usually difficult to identify with any satisfactory degree of certainty, because of their almost innumerable variety and atypical behavior; as in this case, the diagnosis must often be made chiefly on the basis of statistical probability, after as many types as possible have been ruled out or shown to be unlikely, for one reason or another.

For a beginning, we may attempt to determine the probable etiology of the tumor. Two things very strongly rule out an infectious agent, or an inflammatory disease; first, the entire course of the illness was, practically speaking, afebrile; and neither of two blood examinations showed abnormality of the leukocyte count, in spite of the chronicity of the condition. Second, there is every indication that the mass was present at birth, and was the cause of the initial and subsequent episodes of atelectasis. There is nothing to make us suspect the most common congenital infection, syphilis; congenital tuberculosis is not only very rare, but causes a different type of pathology: either a very extensive miliary tuberculosis, or severe tuberculosis of the entire respiratory system, including tuberculous nasopharyngitis and otitis media. There is no reason to expect the remaining few congenital infections to give rise to nothing but an isolated mediastinal granuloma.

We can conclude, therefore, that this tumor was spontaneous in origin; and there are several factors which indicate that it was benign in nature, or at least of a low grade of malignancy. First, the X-rays show none of the density associated with the usually highly cellular malignancies. Second, the displaced trachea is smooth and gently curving; there is no sign of irregularity, lobulation, infiltration or erosion of adjacent structures, or metastasis. Third, there is evidence that there was never any appreciable growth in size. The mass was presumably large enough at birth so that it nearly killed the infant then; if it had grown any larger in the five weeks preceding radiotherapy, it would almost certainly have caused death during this period, in spite of artificial respiration, oxygen, and stimulants. That the tumor finally did cause death was due, I feel, not to its growth, but to an unfortunate change in its position, or to the fact that a respiratory

tree already highly obstructed in its upper part was very susceptible to complete obstruction of a smaller branch by mucus which would normally be easily removed by ciliary action aided by an adequate air current.

Fourth, there was no true response to radiation. Over the period of six weeks during which the mass was observed, it was only once seen to vary more than a millimeter from its original three-by-two-centimeter dimensions; the single exception consisted of a five-millimeter decrease in thickness only, and may have been apparent, due to change in position of the tumor, perhaps secondary to mediastinal shift. With regard to radiosensitivity, it can be noted at this point that lymphosarcomata, lymphocytomata, and leukemic infiltration of the mediastinal nodes melt away almost completely in four to ten days after radiation. Even the tumors of Hodgkin's disease (which has been reported at the age of two months) are considerably reduced ten days after initial radiation and decrease progressively in size, so that they may be apparently gone in six weeks. Neurogenic sarcomata are, however, radioresistant; the most common congenital malignancies are sarcomatous, and the most common tumors of the posterior mediastinum are neurogenic in origin, so that we cannot, on the basis of behavior under X-ray therapy, eliminate neurogenic sarcoma from consideration.

A fifth argument against malignancy, although not as strong as the other points, is the absence of fever and leukocytosis, such as is so often found with those malignant tumors which destroy tissue or undergo partial degeneration by outgrowing their own blood supply.

Finally, because of their great rarity, we can practically exclude pleural and pericardial mesiotheliomata; esophageal rhabdomyoma is likewise extremely rare, if reported at all; parathyroid adenomata and primary thyroid tumors are exceedingly rare in the posterior mediastinum, and the age of the infant should rule out, for practical purposes, bronchiogenic or metastatic carcinoma, there being no demonstrable primary source for the latter, anyway.

I feel, therefore, that this mass was histologically benign. Teratomata (including dermoid cysts) are almost unheard of in the posterior mediastinum, though relatively not uncommon in the anterior mediastinum. In any case, there is no dense wall or calcification to suggest teratoma or dermoid. Lipomata in this region are often very large, but are usually distinctly lobulated and quite radio-opaque. Hemangiomata in the chest are often accompanied by easily identifiable vascular nevi or tumors in more accessible parts of the body, and are often multiple; they very frequently cause erosion when as close to bone as this tumor must be, often give rise to palpable thrills, and usually cause a bruit or soft systolic murmur, said to be heard most often near the costovertebral angles. The recently described vascular ring anomalies cause compression, not displace-

ment, of the trachea and esophagus; I do not know if congenital aortic aneurysm has ever been reported, but would expect one to give most of the classical clinical and roentgenological signs. While neurofibroma cannot be ruled out (it is the most common tumor of the posterior mediastinum, in adults at least, for ganglioneuromata are quite uncommon) I should hardly expect one to be this size at birth, or to be nearly so radiolucent. Finally, of the solid tumors, chondromata of the intervertebral disc are rare; these, as well as osteomata of the vertebral bodies, would cause changes in the spinal column.

Most likely of all, I think, is a congenital cystic structure. Absence of rachischisis rules out anterior meningocele; hygroma colli cysticum generally gives evidence of its presence by appearing in the neck, forms a lobulated mass, seldom descends very far caudad, but can be seen in the superior mediastinum when it does so descend. While pleural and pericardial cysts practically always extend into the lateral chest or the anterior mediastinum, the posterior mediastinum is the location of gastric, enteric, and bronchiogenic mediastinal cysts, and it is on one of these three that my first choice lies.

The mass in this case appears to be predominantly left-sided (the trachea is displaced to the right) and only four of the nineteen reported cases of gastric mediastinal cyst were on the left side; only six mediastinal cysts of enteric origin have been reported. Moreover, such structures usually communicate with the esophagus, into which they intermittently discharge their contents, which may be regurgitated. Far more common are bronchiogenic cysts (these regularly have no communication with the airway when in the mediastinum), which give manifestations identical to those in the case under discussion: continuous or frequent attacks of severe dyspnea and cyanosis, frequent episodes of atelectasis (and often of pneumonia), and often death from asphyxia in the first few months of life. They often cause the equivalent of dysphagia—i.e., the child does not take feedings properly; it either frequently regurgitates food while swallowing, or must be forced to feed, and consequently does not progress well, due to malnutrition. The nurses' notes, in the original case records, indicate that this was true here. Finally, in favor of a bronchiogenic cyst, is the extreme difficulty in X-ray visualization; the mass appears on a single film, taken with special soft-tissue technique, and its outlines are none too clear; on all the other films its location is indicated only by displacement of the trachea.

In conclusion, I should like to repeat that I prefer to make the diagnosis of congenital mediastinal cyst, of bronchiogenic origin. The possibility that the reported slight decrease in size after radiotherapy was real rather than apparent makes neurogenic sarcoma of low-grade malignancy a second choice.